Recent Developments in Treatment of Pulmonary Diseases

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ONE of the most important advances in chest diseases in recent years has been the advent of streptomycin in the treatment of pulmonary tuberculosis. Although its discovery was announced only four years ago, experience with over one thousand patients in Army, Navy, Veterans, and civilian hospitals has clearly demonstrated that streptomycin alters the course of tuberculous infections in a manner unapproached by earlier chemotherapeutic agents.[3,7]

Exudative infiltrations of recent origin represent the type of pulmonary lesion most favorably influenced by streptomycin. At this stage vascularity remains little impaired, and there is good penetration of the antibiotic throughout the involved tissues. The most dramatic results are observed in miliary tuberculosis, in which there is frequently complete roentgenologic clearing of the pulmonary infiltrations. Relapses unfortunately occur in the majority of such patients, and a second course of treatment is ineffective because of the appearance of resistant organisms. Another reason for the poor results obtained in miliary tuberculosis is the high incidence of tuberculous meningitis, which may be present when treatment is started, or may develop two or three months later. With tuberculous meningitis the initial response to treatment is also usually good, but later the signs and symptoms recur and death results within a few weeks. Only about 15 per cent of patients with tuberculous meningitis have remained symptom free for as long as a year following therapy with streptomycin.

Because of the development of resistant organisms, and the toxic potentialities of the drug, it is generally felt that streptomycin is not indicated at present in the treatment of patients with minimal and moderately advanced pulmonary tuberculosis, since in these stages the response to bed rest and collapse therapy is usually favorable. Streptomycin is also contraindicated in chronic fibroid or fibrocaseous tuberculosis, in which anatomical barriers prevent adequate contact between the infecting organisms and the antimicrobial agent. There may be regression of the infiltration surrounding long-standing fibrocaseous involvement, but improvement is usually slight and temporary. Tuberculous empyema is not benefited by streptomycin.

Streptomycin also seems to be of value when used in conjunction with the surgical treatment of tuberculosis, especially resection. In the recent series of Clagett,[2] streptomycin appeared to prevent early postoperative spreads following lobectomy and pneumonectomy. Late spreads, however, were not prevented. The role of resection in the treatment of pulmonary tuberculosis is not finally established, but preliminary experience indicates that streptomycin will prevent at least some of its hazardous complications. Streptomycin may also be used in conjunction with thoracoplasty, to prepare the patient for operation, and for the treatment of postoperative spreads. Other surgical procedures, such as extrapleural pneumonolysis, are being re-evaluated in the hope that streptomycin will decrease complications.

A disturbance of function of the inner ear is the chief toxic manifestation caused by streptomycin. This occurs in virtually every patient who receives daily doses of 2 gm. or more for three or four weeks, and causes unsteadiness and dizziness, which is usually mild, but may be incapacitating. The damage to the vestibular apparatus is apparently permanent, but except in elderly individuals compensatory mechanisms are so effective that the disability is not noticed after a few weeks. Sensitivity reactions, chiefly fever, rashes, and eosinophilia, are common but usually of no consequence. Other serious toxic manifestations such as deafness, renal damage, exfoliative dermatitis, and agranulocytosis, are fortunately rare. Aside from toxicity, the main limitation to streptomycin therapy is the development of resistant organisms. The majority of patients treated with daily doses of 2 gm. or more of the antibiotic have developed highly resistant organisms within three or four months, and sometimes as early as the sixth or eighth week. Clinical experience has demonstrated that when resistant tubercule bacilli appear in the test tube, the patient no longer responds to the action of the drug.

Following empirical trials with 2 or 3 gm., it has been found that equally good results are obtained in pulmonary tuberculosis with 1 gm. daily, or less, given in two or three divided doses. Recent evidence indicates that these smaller doses are associated with decreased toxicity and with a lower incidence of development of resistant organisms.

OTHER PULMONARY INFECTIONS

Streptomycin is also remarkably effective in the treatment of a variety of non-tuberculous pulmonary infections. Pleuropulmonary tularemia is perhaps the most noteworthy example. Morgan[8] reports gratifying results in 27 patients, and emphasizes the value of early diagnosis and treatment. Since the diagnosis is often made by a rising agglutinin titer during the second or third week of illness, early treatment on the basis of the clinical picture is advised in regions where tularemia is endemic.

Friedlander's pneumonia also responds well to streptomycin therapy. Here again treatment must be started early, because of the tendency of this infection to cause extensive tissue destruction and abscess formation. Hemophilus influenza pulmonary

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infections should be treated with both streptomycin and sulfadiazine; striking results have been obtained in the relatively small number of cases so far reported. Pasteurella pestis is highly susceptible to streptomycin, and the recently published animal experiments of Meyer and his associates at the University of California suggest that its use will markedly decrease the mortality from pneumonic plague.[10] Brainerd[1] of San Francisco has found in a small number of cases that streptomycin appears to be at least as effective as hyperimmune serum in the treatment of severe whooping cough.

The response obtained in these infections, caused by Gram negative organisms, makes a prompt and precise bacteriological diagnosis more imperative than ever before. Identification takes two or three days, so that when there is any doubt, as for example when direct smears of the sputum show a predominance of Gram negative organisms, sulfadiazine or streptomycin should be administered from the outset. If the drug is given in doses of 1 to 2 gm. daily for only a few days, the toxicity of streptomycin is negligible, and it can be promptly discontinued if the infection is found to be caused by organisms more susceptible to penicillin.

The role of penicillin in the treatment of pulmonary infections is now so well established that it need be mentioned only briefly. The treatment of pneumococcic and other bacterial pneumonias, with or without empyema, has been revolutionized by the advent of this virtually nontoxic agent. Curiously, one virus infection of the respiratory tract, psittacosis, is suspectible to penicillin. Brainerd[1] has treated eight patients with psittacosis, mostly acquired as laboratory infections, and reports prompt subjective and objective improvement, with complete clearing of the pulmonary infiltrations within a few weeks. The majority of lung abscesses can now be cured by medical means alone, and in the chronic cases requiring surgical drainage or resection, the administration of penicillin greatly reduces postoperative complications. In bronchiectasis penicillin is of invaluable aid in treating intercurrent pneumonias, in enabling otherwise incapacitated individuals to gain weight and return to work, and in the pre- and postoperative management of cases suitable for lobectomy or pneumonectomy. The safety with which all surgical operations in the chest can be undertaken has been greatly enhanced by the newer antimicrobial agents, and especially penicillin.

LUNG TUMORS

Increased interest is being shown in the diagnosis and treatment of lung tumors, especially carcinoma of the lung. Formerly considered a rare malignancy with a hopeless prognosis, this tumor is now known to make up about 10 per cent of all carcinomas. Efforts toward early diagnosis and treatment have yielded encouraging results.

Approximately 80 per cent of carcinomas of the lung occur in men over 40 years of age. In this age group cough, chest pain, hemoptysis, persistent respiratory infections, or abnormal densities on the chest x-ray, should be regarded as manifestations of carcinoma of the lung until proved otherwise. The diagnosis can be established in less than half the cases by bronchoscopy and biopsy. Examination of sputum or bronchial secretions for tumor cells, stained by the Papanicolaou method, represents an important new aid in this respect, for its use permits a definite cytologic diagnosis in over 80 per cent of cases.[5,6] An added advantage of the smear examination is that slides can be prepared by local physicians in outlying communities and sent to centers where there are specialists in cellular morphology. Such a center has been established at the University of California.

The treatment of carcinoma of the lung is resection, usually pneumonectomy. Recent advances in anesthesiology and surgical technic, as well as the advent of the antibiotics, have greatly decreased the operative hazards. In Ochsner's recently published series the surgical mortality for carcinoma of the lung was 46.4 per cent prior to 1942, and only 19.3 per cent since then.[9] Of the patients who underwent resection over five years ago, 23.3 per cent are still alive. Thus, although many patients with carcinoma of the lung are seen after the tumor has reached an inoperable stage, the outlook is much more hopeful in cases in which the diagnosis is made early.

Exploratory thoracotomy, which in skilled hands is now felt to be no more dangerous than exploratory laparotomy, is being resorted to with increasing frequency in the management of mediastinal and parenchymal shadows of unknown cause. Davis, for example, recently did exploratory thoracotomies in 40 patients to find the cause of silent spherical shadows, and found that in 70 per cent of the cases they were caused by malignant tumors.[4] Mediastinal enlargements, when bilateral, may be observed during an initial period of radiation therapy if the clinical picture is suggestive of a lymphoma. If the enlargement is unilateral, thoracotomy is usually indicated without delay if an infectious process can be ruled out and the results of other diagnostic procedures are negative. Angiocardiography is most helpful in ruling out aneurysms and other vascular abnormalities. Keen clinical judgment is needed, but most authorities are now agreed that an aggressive policy toward exploratory thoracotomy is one of the chief methods of decreasing the mortality rate from pulmonary neoplasms.

SUMMARY

Streptomycin and other antimicrobial agents have revolutionized the treatment of pulmonary infections, including tuberculosis, and have greatly decreased the hazards of surgical operations on the chest. Notable advances have also been made in the diagnosis and treatment of lung tumors.

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The Surgical Treatment of Cancer

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SURGICAL treatment offers the only hope of cure for most malignant tumors. It can be effectively combined with roentgen and radium therapy in organs such as the thyroid or uterus. Complete extirpation of the malignant process will result in cure. Unfortunately, good results follow operation only when the malignant lesion is confined to its primary site, while too often patients are submitted to operation at a stage in the disease when local extension, regional node involvement and distant metastases are already present. The percentage of so-called five-year cures is reduced to a low figure when extension has occurred, although palliative benefits in the form of increased comfort and possible prolongation of life may be obtained.

Progress continues to be made year by year in technical procedures for the removal of malignant tumors, and new fields of surgery have been developed in recent years which permit the removal of cancer in locations difficult of access. Improved methods, new operative procedures, better preparation of patients for operation, widespread use of blood, transfusions, improved anesthesia and the use of antibiotics all have aided in the reduction of mortality following the extensive operative procedures necessary for the removal of malignant growths. Further technical improvements will continue to be made year by year, yet they have not appreciably changed the curability rate of malignancies such as those occurring in the esophagus, stomach or lung.

In order to improve the results of surgery in cancer we must look to some other means than possible technical improvements in operations. Since the surgical results are dependent upon the stage to which the malignancy has developed, it is essential that the major effort be directed toward earlier diagnosis at a time when the malignancy is confined to its primary site. This attack on the cancer problem has taken several directions, most of which have been helpful. Education of the public has now been conducted for many years, yet in recent surveys of large groups of patients with cancer, the delay of the patient in seeking medical advice after being aware of symptoms was shown to be still several months. A continuation of this program of lay education is necessary and essential for earlier diagnosis.

The delay in patients reaching operation is not entirely the fault of the patient and a real responsibility for it must be accepted by us as physicians. Due to inadequate or incomplete examination, a correct diagnosis in many cases is arrived at only weeks or months after the patient first consults his physician with definite symptoms suggesting the possibility of malignancy. An attempt is being made this year under the auspices of the American Cancer Society, American College of Surgeons and state medical societies to establish cancer detection centers for the examination of patients without symptoms to try to get earlier diagnoses. Experiences so far with cancer detection centers have not been encouraging. Few patients with cancer will be discovered by this means, a large expense is involved and it seems wiser that these examinations be done by the individual physician in the course of a general examination for the discovery of any disease as well as cancer. "Pilot" cancer detection centers in order to determine just what is necessary for an examination for the detection of a malignancy can be useful, since by this

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